REMARKS

Applicants' claim to priority has been acknowledged. Applicants' petition is acknowledged and it is Applicants' understanding that the petition will be processed subsequent to the transmittal of the present Office Action. Claims 43-44 and 47-54 are presently under consideration. Claims 43 and 50 have been amended to more clearly set forth aspects of the invention. Claim 51 has been amended to correct a minor typographical error. New claim 55 is presented herein. Accordingly, claims 43, 50, and 51, as amended, and dependent claims therefrom, and new claim 55 are under consideration.

Support for the amendments to the claims is found throughout the specification and in the original claims. Specifically, support for the amendment to claim 43 is presented in the specification at page 13, lines 9-11, wherein support for distinct optically resolvable polynucleotides is found; at page 20, lines 10-15; at page 22, lines 3-9, wherein the correlation between single molecule fluorescence and single step photobleaching is described; and in Figure 3, which shows an emission spectra exemplifying single step photobleaching and reveals experimental evidence depicting single molecule fluorescence. Support for the amendment to claim 43 is also found in Example 4, at page 26, line 26 to page 27, line 30, wherein the single step photobleaching feature of the array of the present invention is reduced to practice. Support for the amendment to claim 50 is found in claim 50 as previously presented. No issue of new matter is introduced by the amendments to the claims.

Support for new claim 55 is found throughout the specification and in the original claims. Specifically, support for new claim 55 is found, for example, at page 10, lines 14-25; and at page 15, lines 10-15, wherein arrays comprising genomic DNA fragments are described. No issue of new matter is introduced by this amendment.

Rejections under 35 USC § 102

Claims 43, 44, 47, 50, 51, 53, and 54 have been rejected under 35 USC § 102(a) as allegedly anticipated by Gunderson *et al.* (EP 0995804, published 26 April 2000). In view of the amendments to the claims and applicants' arguments hereinbelow, the rejection, as it applied to claims 43, 44, 47, 50, 51, 53, and 54, is respectfully traversed.

Out the outset, Applicants' note that the Gunderson *et al.* patent application was published after the priority date to which the present application is entitled. Applicants, therefore, believe that this reference is inappropriately cited as prior art with regard to the present invention.

Claims 43, 44, 47, 50, 51, and 53 have been rejected under 35 USC § 102(b) as allegedly anticipated by Lockhart *et al.* (WO 97/27317, published 13 July 1997). Upon consideration of the amendments to the claims and applicants' arguments, the rejection of claims 43, 44, 47, 50, 51, and 53, is respectfully traversed.

Claims 43, 44, 47, 50, 51, and 53 have been rejected under 35 USC § 102(b) as allegedly anticipated by Lane *et al.* (WO 97/08183, published 6 March 1997). This rejection is respectfully traversed in view of the amendments to the claims and applicants' arguments presented hereinbelow.

Applicants assert that none of these references (i.e., Gunderson *et al.*, Lockhart *et al.*, or Lane *et al.*) teach or suggest a distinctive structural feature of the array of the present invention, namely that the plurality of nucleic acids are distinct optically resolvable polynucleotide molecules immobilized on a solid surface, and each polynucleotide molecule is individually resolvable and detectable as a **single molecule fluorescent point**, wherein fluorescence from said single molecule fluorescent point exhibits **single step photobleaching**. *Emphasis added.* Inasmuch as each of Gunderson *et al.*, Lockhart *et al.*, and Lane *et al.* fail to teach the structural feature of a single molecule fluorescent point detectable by single point photobleaching as recited in the presently amended claims, these references are not anticipatory of the present invention.

Moreover, unlike the arrays of the present invention, the arrays described by Gunderson *et al.*, Lockhart *et al.*, and Lane *et al.* are characterized by closely packed clusters of substantially identical nucleic acid molecules. As indicated in the specification at page 5, lines 26-28, the term "single molecule" is used to distinguish the arrays of the present invention from high density arrays of the prior art, which comprise distinct **clusters** of many molecules of the same type. *Emphasis* added. Moreover, the term "individually resolved" is used to indicate that, when visualized, it is possible to distinguish one molecule on the array from its neighboring molecules. See page 5, lines 29-30. One of skill in the art would appreciate that it is not feasible to

distinguish one molecule on an array from its neighboring molecules when the individual molecule is packed in a cluster comprised of a plurality of like molecules which constitute its molecular neighbors. Indeed, such clusters may comprise thousands of similar molecules, which are detectable on the level of the cluster, not the individual molecule.

Of note, clusters of substantially identical nucleic acid molecules do not exhibit single point photobleaching under standard operating conditions used to detect/analyze nucleic acid molecules on arrays. The intensity of a single molecule fluorescence spot is constant for an anticipated period of time, after which it disappears in a single step. In contrast, the intensity of a fluorescence spot comprised of two molecules, for example, disappears in two distinct and observable steps. The intensity of a fluorescence spot arising from a cluster consisting of thousands of similar molecules, such as those present on the arrays of Gunderson *et al.*, for example, would disappear in a pattern consistent with an exponential decay. The exponential decay pattern reflects the progressive loss of fluorescence by molecules present in the cluster and reveals that, over time, fewer and fewer molecules in the spot retain their fluorescence.

Evidence of this distinctive structural feature of the present invention is depicted in Figure 3, which shows the photobleaching profile of a single DNA molecule containing a single fluorophore attached to a non-fluorescent, surface bound bead. The bead acts as a marker to locate the position of the fluorescent molecules. See Figure 2 for a schematic. In brief, the bead was located using a low power light microscope as described in the specification. The light was then switched off and the fluorescence profile of the DNA was subsequently monitored using a focused laser beam that was switched onto the bead 0.5 seconds after commencement of recording the signal from the fluorescently labeled DNA bound to the bead.

Consistent with expectations for a single fluorophore (i.e., a single molecule fluorescent point), the fluorescence emission was constant for a period of 100 milliseconds after laser illumination (>10 recording events), after which time the fluorescence decayed in a single step. The instant application, therefore, presents experimental evidence of a distinct structural feature of the present invention, that is, a single molecule fluorescent point detectable by single step photobleaching.

In view of the above arguments, the Examiner is respectfully requested to reconsider the validity of the rejection of the claims under 35 U.S.C. §102 and withdraw the rejection.

Rejections under 35 USC § 103

Claims 48, 49, and 52 have been rejected under 35 USC § 103(a) as allegedly unpatentable over Lane *et al.* (WO 97/08183, published 6 March 1997) in view of Lockhart *et al.* (WO 97/27317, published 13 July 1997).

Claims 48, 49, and 52 have been rejected under 35 USC § 103(a) as allegedly unpatentable over Gunderson *et al.* (EP 0995804, published 26 April 2000).

Claims 48, 49, and 52 have been rejected under 35 USC § 103(a) as allegedly unpatentable over Lockhart *et al.* (WO 97/27317, published 13 July 1997).

In that the grounds for rejection of the claims as allegedly obvious in view of the cited references are essentially similar to the rejection of the claims as allegedly anticipated by these references, the amendments and arguments presented hereinabove with regard to the 35 USC § 102 rejection are applicable to the rejection under 35 USC § 103. Accordingly, the rejection of claims 48, 49, and 52 under 35 USC § 103 is respectfully traversed. Applicant submits that the distinct structural feature of the present invention, as described in detail hereinabove, is not obvious in view of any one or a combination of Lane *et al.*, Lockhart *et al.*, and/or Gunderson *et al.*

Power of Attorney

As the undersigned has been asked to take over prosecution of the present application, appropriate documents making the change of record have been executed and are enclosed herewith. Entry and favorable action on these documents is accordingly solicited.

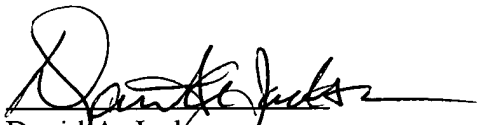
Fees

No additional fees are believed to be necessitated by this amendment. However, should this be an error, authorization is hereby given to charge Deposit Account No. 11-1153 for any underpayment or to credit any overpayment.

Conclusion

It is submitted, therefore, that the claims are in condition for allowance. No new matter has been introduced. From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order, and such action is earnestly solicited. In the event that there are any questions concerning this amendment, or application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of this application may be expedited.

Respectfully submitted,



David A. Jackson
Attorney for Applicant(s)
Registration No. 26,742

KLAUBER & JACKSON
411 Hackensack Avenue
Hackensack, New Jersey 07601
(201) 487-5800

November 11, 2003